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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/048,186	06/19/2002	James C Liao	06497-013002	2905
7590	11/18/2004			
Fish & Richardson 225 Franklin Street Boston, MA 02110-2804				
EXAMINER PROUTY, REBECCA E				
ART UNIT		PAPER NUMBER		
1652				

DATE MAILED: 11/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/048,186

Applicant(s)

LIAO, JAMES C

Examiner

Rebecca E. Prouty

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5,10-13,17,21-24,28,29,33-35,37,38,40,41 and 45-52 is/are pending in the application.
- 4a) Of the above claim(s) 11,22,23,28,37,38 and 46-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5,10,12,13,17,21,24,29,33-35,40,41 and 45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>6/04</u> . | 6) <input type="checkbox"/> Other: _____ |

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Claims 2-4, 6-9, 14-16, 18-20, 25-27, 30-32, 36, 39, and 42-44 have been canceled. Claims 1, 5, 10-13, 17, 21-24, 28, 29, 33-35, 37, 38, 40, 41, 45-48 and newly presented claims 49-52 are still at issue and are present for examination.

Applicants' arguments filed on 8/26/04, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Applicant's election with traverse of Group I, Claims 1, 5, 10-13, 17, 21, 24, 28, 29, 33-35, 37, 38, 40, 41, 45 and new claims 51-52 and of *glnAp2* as promoter species and isopentenyl diphosphate isomerase (*idi*) as heterologous polypeptide in the response filed 12/5/03 is acknowledged. This restriction requirement was made FINAL in the previous Office Action, yet applicants continue to traverse by arguing that the generic claims within group I have been amended such that they are patentable over the prior art and thus the withdrawn species should now be examined. This is not persuasive because the generic claims as amended still do not define an group of claims linked by a special technical feature as defined by PCT Rule 13.2. The only shared technical feature linking all claims within Group I is that they all require a nucleic acid encoding

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a heterologous enzyme linked to a promoter bound by ntrC and functional in *E. coli*. However, this shared technical feature is not a special technical feature because Schroeckh et al. (Reference AP of applicant's PTO-1449) teach the linking of the *E. coli glnAp2* promoter to a heterologous enzyme for recombinant production of the enzyme. Furthermore, even if one considered the limitation of the claims to the heterologous enzyme being selected from a biosynthetic enzyme for production of an isoprenoid, a polyketide, or a polyhydroxyalkanoate, there is no special technical feature linking all claims in view of the disclosure of Schroeckh et al. as the it would have been obvious for one of skill in the art to select a biosynthetic enzyme for production of an isoprenoid, a polyketide, or a polyhydroxyalkanoate as the heterologous enzyme as the recombinant production of these enzymes is well known in the art to be important for the production of carotenoids, polyketide antibiotics and other medically and industrially important compounds. As such even in view of the amendments to the claims the election of species requirement remains proper.

Claims 11, 22, 23, 28, 37-38 and 46-52 are withdrawn from further consideration pursuant to CFR 1.142(b) as being drawn to a nonelected invention (Claims 22, 23 and 46-50) or species (Claims 11, 28, 37, 38, 51 and 52), there being no allowable

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generic or linking claim. Note Claims 11 and 28 correspond to a non-elected species gene as the metabolite synthesized by the elected idi gene is dimethylallyl diphosphate (DMAPP) which is not a carotenoid as required by these claims. Claims 1, 5, 10, 12, 13, 17, 21, 24, 29, 33-35, 40, 41 and 45 are examined herein.

Claim 24 is objected to because of the following informalities: the word "the" should be inserted prior to "glnL gene" in line 5. Appropriate correction is required.

Claims 10, 12, 13, 17, 21, 40, 41 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 45 is incomplete as dependent on canceled Claim 42. For purposes of examination, this claim is interpreted as if dependent from Claim 24.

Claim 40 (from which claim 41 depends) is confusing in the recitation of "promoter that is bound by ntrC and acetyl phosphate" as the specification does not identify any promoter that is bound by acetyl phosphate. While the specification describes promoters that are regulated by acetyl phosphate, this regulation is effected through the a response regulator protein and not by direct binding of acetyl phosphate to the promoter.

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For purposes of examination, it is assumed that applicants intent was to recite "promoter that is bound by ntrC and regulated by acetyl phosphate"

Claim 10 (from which claims 12, 13, 17 and 21 depend) is confusing in the recitation of "first enzyme that catalyzes biosynthesis of an isoprenoid ... and ... a second enzyme that catalyze biosynthesis of the isoprenoid" as this appears to recite a cell encoding two different enzymes that catalyze the synthesis of the **same** isoprenoid by different reactions but applicants intent instead appears to be to recite a cell encoding two enzymes which catalyze separate reactions in a biosynthetic pathway for a single desired isoprenoid. Although applicants appear to believe that the amendments to the claims have clarified this problem, this is not the case as the claims clearly says that the second enzyme catalyzes biosynthesis of **the** isoprenoid, i.e., the same compound synthesized by the first enzyme.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 10, 12, 13, 21, 29, and 33-35 rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Schroeckh et al. (Reference AP of applicant's PTO-1449), Kajiwara et al. (1997) and Bock et al. (US Patent 5,830,692).

Schroeckh et al. teach the use of the *E. coli* glnAP₂ promoter for the recombinant production of heterologous proteins in *E. coli*. Schroeckh et al. teach that this promoter is tightly regulated by the nitrogen concentration and capable of producing similar amounts of recombinant protein as other well known *E. coli* promoters.

Kajiwara et al. teach constructs for the recombinant expression of isopentenyl diphosphate isomerase (idi) in *E. coli* cells producing carotenoid metabolites and that the increased expression of idi is useful for increasing the amount of carotenoids produced. The constructs of Kajiwara et al. comprise the idi gene under the control of the inducible lac promoter. (see Fig 1).

Bock teach that inducible promoters such as lac, tac, and trp promoters possess several disadvantages in relation to their use for industrial production. These are that the repressors and inducers necessary for use of these promoters are expensive

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and difficult to handle, particularly when they are metabolizable substances (such as lactose and tryptophan), and cannot be induced completely when the repressor is present in molar excess. (see columns 1-2).

Therefore, it would have been obvious to one of ordinary skill in the art to replace the lac promoter of the constructs of Kajiwara et al. with the *E. coli* glnAP₂ promoter of Schroeckh et al. as this promoter can be easily regulated without any expensive inducer.

The previous rejection of the claims under 35 U.S.C. 103(a) as being unpatentable over Liao (WO96/08567) in view of Bock et al. (US Patent 5,830,692), McCleary et al. (Reference AL of applicant's PTO-1449), McCleary et al. (Reference AM of applicant's PTO-1449) and Haldiman et al. (Reference AK of applicant's PTO-1449) or Feng et al. (Reference AJ of applicant's PTO-1449) is withdrawn as all claims have been limited to a biosynthetic enzyme for production of an isoprenoid, a polyketide or a polyhydroxyalkanoate as the heterologous enzyme. As phosphoenol pyruvate synthase does not meet this limitation this rejection is withdrawn.

The previous rejection of the claims under 35 U.S.C. 103(a) as being unpatentable over Kajiwara et al. (1997) in view of Bock et al. (US Patent 5,830,692), McCleary et al. (Reference AL

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of applicant's PTO-1449), McCleary et al. (Reference AM of applicant's PTO-1449) and Haldiman et al. (Reference AK of applicant's PTO-1449) or Feng et al. (Reference AJ of applicant's PTO-1449) is withdrawn in view of applicants arguments that one of skill in the art would not have been motivated to link the production of idi to the production of acetate because acetate was known to be detrimental to the growth of cells. While the skilled artisan would have expected that the expression of idi would reduce the acetate production as the action of idi would increase the flow of carbon into the carotenoid biosynthetic pathway and thus away from acetate production, one of skill in the art would not have necessarily expected that this would be sufficient to alleviate the detrimental effects of acetate and that one could achieve sufficient levels of production of carotenoids under these conditions.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5, 10, 12, 13, 17, 21, 24, 29, 33-35, 40, 41 and 45 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-40 of US Patent 6,706,516. The rejection was explained in the previous Office Action.

This rejection is no longer a provisional rejection in view of the issuance of parent application 09/626,612 as US Patent 6,706,516. Applicant's statement that a terminal disclaimer may be filed is noted but the rejection will be maintained until the disclaimer is filed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action

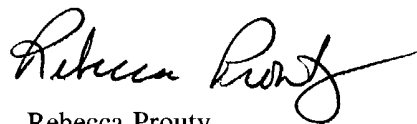
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is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.



Rebecca Prouty
Primary Examiner
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